REMARKS

Claims 1-34 are presently pending in this application and have been subject to restriction as follows:

I. Claims 1-12, and 18-34 drawn to nucleic acid molecules, vectors, compositions and cells comprising a nucleic acid molecule, classified in class 435, subclass 325.

II. Claims 13-17 drawn to a method of producing a chimeric RNA molecule in a cell, classified in class 435, and subclass 6.

In support of the present restriction requirement, the Examiner has alleged that the subject matter of the pending claims represent distinct inventions.

In particular, the Examiner alleges that Inventions I and II are related as product and process of use. According to the Examiner, the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). The Examiner maintains that in the instant case the nucleic acid molecules, vectors and cells recited in invention I can be used for a materially different method other than the methods set forth in invention II. For example the nucleic acid molecules of Invention I can be used for producing proteins encoded by the *trans*-spliced gene products encoded by the nucleic acid molecules comprised within the respective nucleic acid molecules according to Invention I.

The Examiner concludes that because the inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The requirement for restriction is respectfully traversed for a number of reasons. First, there is clearly a structural and functional relationship between the claims of Group I and II. Specifically, the claims of groups I and II directly relate to compositions and methods for targeting *trans*-splicing to a factor VIII pre-mRNA for the purpose of expressing a chimeric factor VIII mRNA.

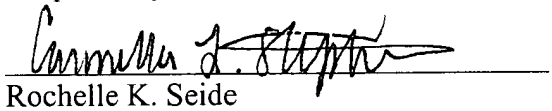
Second, contrary to the Examiner's contention the nucleic acid molecules, vectors and cells of Group I are not designed to be used for the production of proteins encoded by the claimed nucleic acid molecule. In fact, the claimed nucleic acid molecules of Group I have no use independent from their ability to mediate a *trans*-splicing reaction which results in the production of a chimeric RNA molecule (Group II claims) which results in expression of a factor VIII polypeptide. In other words, the process for using the product as claimed **cannot** be practiced with another materially different product **and** the product as claimed **cannot** be used in a materially different process of using that product.

Moreover, Applicant's respectfully direct the Examiner's attention to the claims of U.S. Patent No: 6,280,978 ("the '978 patent"), a patent to which the present application claims priority. The claims are attached herewith as Exhibit A. A review of the claims issued in the '978 patent demonstrates that the Patent and Trademark Office had previously determined that claims to compositions capable of targeting binding to a pre-mRNA and methods for producing a chimeric RNA molecule in a cell utilizing such compositions were considered a single invention.

Finally, given the relationship between the subject matter encompassed by the pending claims of Groups I and II, Applicants assert that there would not be an undue search burden to examine the pending claims as a single group.

However, in order to be fully responsive to the requirement for restriction, Applicants elect, with traverse, the claimed nucleic acid molecules, vectors, compositions and cells of Group I. Withdrawal of the requirement for restriction and favorable consideration and allowance is earnestly solicited.

Respectfully submitted,



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<210> SEQ ID NO: 67
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<210> SEQ ID NO: 68
<211> LENGTH: 37
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<213> ORGANISM: Artificial Sequence
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We claim:

1. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

2. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

3. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

4. The cell of claim 1 wherein the nucleic acid molecule further comprises a 5' donor site.

5. The cell of claim 1 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

6. The cell of claim 1 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary base pairing, triple helix formation, or protein-nucleic acid interaction.

7. The cell of claim 1 wherein the nucleotide sequence to be trans-spliced to the target pre mRNA encodes a translatable cystic fibrosis trans-membrane conductance regulator polypeptide.

8. The cell of claim 1 wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exon 10 of the cystic fibrosis trans-membrane conductance regulator protein.

9. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

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<400> SEQUENCE: 66

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<210> SEQ ID NO: 67
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
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<400> SEQUENCE: 68

gcagtgtcct tgtgcggtta ccctgcaggg cggcttc 37

We claim:

1. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

2. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

3. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

4. The cell of claim 1 wherein the nucleic acid molecule further comprises a 5' donor site.

5. The cell of claim 1 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

6. The cell of claim 1 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary base pairing, triple helix formation, or protein-nucleic acid interaction.

7. The cell of claim 1 wherein the nucleotide sequence to be trans-spliced to the target pre mRNA encodes a translatable cystic fibrosis trans-membrane conductance regulator polypeptide.

8. The cell of claim 1 wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exon 10 of the cystic fibrosis trans-membrane conductance regulator protein.

9. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

10. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

11. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane membrane conductance regulator pre-mRNA expressed within the cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

12. The cell of claim **9** wherein the nucleic acid molecule further comprises a 5' donor site.

13. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

14. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

15. A method of producing a chimeric RNA molecule in a cell comprising: contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within the cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be tran-spliced to the targer pre-mRNA;

wherein a chimeric RNA molecule is produced within the cell.

16. A method of claim **13** wherein the nucleic acid molecule further comprises a 5' donor site.

17. The method of claim **13**, wherein the chimeric RNA molecule comprises sequences encoding a translatable protein.

18. A nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within a cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain;

d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and

e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

19. A nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within a cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain;

d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and

e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

20. A nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within a cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain;

d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site; and

e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

10. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

11. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane membrane conductance regulator pre-mRNA expressed within the cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

12. The cell of claim **9** wherein the nucleic acid molecule further comprises a 5' donor site.

13. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

14. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance regulator pre-mRNA expressed within the cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

15. A method of producing a chimeric RNA molecule in a cell comprising: contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within the cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be tran-spliced to the targer pre-mRNA;

wherein a chimeric RNA molecule is produced within the cell.

16. A method of claim **13** wherein the nucleic acid molecule further comprises a 5' donor site.

17. The method of claim **13**, wherein the chimeric RNA molecule comprises sequences encoding a translatable protein.

18. A nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within a cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain;

d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and

e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

19. A nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within a cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain;

d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and

e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

20. A nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis transmembrane conductance regulator pre-mRNA expressed within a cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain;

d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site; and

e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

21. The nucleic acid molecule of claim **18** wherein the nucleic acid molecule further comprises a 5' donor site.

22. The nucleic acid molecule of claim **18** wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary base pairing, triple helix formation, or protein-nucleic acid interaction.

23. The nucleic acid molecule of claim **18** wherein the nucleotide sequences to be trans-spliced to the target pre-mRNA encode a translatable cystic fibrosis trans-membrane conductance regulator polypeptide.

24. The nucleic acid molecule of claim **18** wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exon 10 of the cystic fibrosis trans-membrane conductance regulator protein.

25. The nucleic acid molecule of claim **20** wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary base pairing, triple helix formation, or protein-nucleic acid interaction.

26. The nucleic acid molecule of claim **20** wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes a translatable cystic fibrosis trans-membrane conductance polypeptide.

27. The nucleic acid molecule of claim **20** wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exon 10 of the cystic fibrosis trans-membrane conductance regulator protein.

28. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance protein pre-mRNA expressed within a cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

29. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance protein pre-mRNA expressed within a cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

30. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance protein pre-mRNA expressed within a cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

31. The vector of claim **28** wherein the nucleic acid nolecule further 5' donor site.

32. A composition comprising a physiologically acceptable carrier and a nucleic molecule according to any claims **28–31**.

* * * * *

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

21. The nucleic acid molecule of claim **18** wherein the nucleic acid molecule further comprises a 5' donor site.

22. The nucleic acid molecule of claim **18** wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary base pairing, triple helix formation, or protein-nucleic acid interaction.

23. The nucleic acid molecule of claim **18** wherein the nucleotide sequences to be trans-spliced to the target pre-mRNA encode a translatable cystic fibrosis trans-membrane conductance regulator polypeptide.

24. The nucleic acid molecule of claim **18** wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exon 10 of the cystic fibrosis trans-membrane conductance regulator protein.

25. The nucleic acid molecule of claim **20** wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary base pairing, triple helix formation, or protein-nucleic acid interaction.

26. The nucleic acid molecule of claim **20** wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes a translatable cystic fibrosis trans-membrane conductance polypeptide.

27. The nucleic acid molecule of claim **20** wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exon 10 of the cystic fibrosis trans-membrane conductance regulator protein.

28. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance protein pre-mRNA expressed within a cell;

b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

29. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance protein pre-mRNA expressed within a cell;

b) a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

30. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a cystic fibrosis trans-membrane conductance protein pre-mRNA expressed within a cell;

b) a 5' splice site;

c) a spacer region that separates the 5' splice site from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

31. The vector of claim **28** wherein the nucleic acid nolecule further 5' donor site.

32. A composition comprising a physiologically acceptable carrier and a nucleic molecule according to any claims **28–31**.

* * * * *